

The background of the slide features a close-up, shallow depth-of-field photograph of a person's hand holding a blue pipette. The pipette is positioned over a white multi-well plate, with a single drop of blue liquid being dispensed into one of the wells. The lighting is bright and clinical, highlighting the textures of the skin and the glass of the plate.

**NEKTAR**<sup>®</sup>

NEW PATHWAYS TO  
SMARTER MEDICINE™

# **Cowen & Company 38<sup>th</sup> Annual Health Care Conference**

Jonathan Zalevsky, Ph.D.  
Senior Vice President and  
Chief Scientific Officer

March 14, 2018

This presentation includes forward-looking statements regarding Nektar's proprietary drug candidates, the timing of the start and conclusion of ongoing or planned clinical trials, the timing and outcome of regulatory decisions, and future availability of clinical trial data. Actual results could differ materially and these statements are subject to important risks detailed in Nektar's filings with the SEC including the Form 10-K filed on March 1, 2018. Nektar undertakes no obligation to update forward-looking statements as a result of new information or otherwise.

# Focus of Nektar Pipeline

## Immuno-oncology

Target the innate and adaptive immune system

### NKTR-214

(Co-Develop and Co-Promote)

#### CD122-Biased Agonist

- Multiple Solid Tumors
- In Phase 1/2 Trials*



### NKTR-262 (Wholly-Owned)

#### TLR 7/8 Agonist

- Multiple Solid Tumors
- IND Filed, Phase 1 Dosing to Start Q1 2018*

### NKTR-255 (Wholly-Owned)

#### IL-15 Receptor Agonist

*IND in Early 2019*

## Immunology

Harness the immune system to fight auto-immune disease

### NKTR-358 (Co-Promote)

#### T Regulatory Cell Stimulator

- Lupus
- Crohn's Disease
- Rheumatoid Arthritis
- Psoriasis

#### *In Phase 1 Studies:*

- *SAD ongoing*
- *MAD in Lupus patients Q2 2018*



## Chronic Pain & Opioid Epidemic

Help prevent the next generation of opioid addiction

### NKTR-181 (Wholly-Owned)

#### New Opioid Agonist Molecule

- Separates analgesia from euphoria that leads to abuse and addiction
- Moderate to Severe Chronic Pain

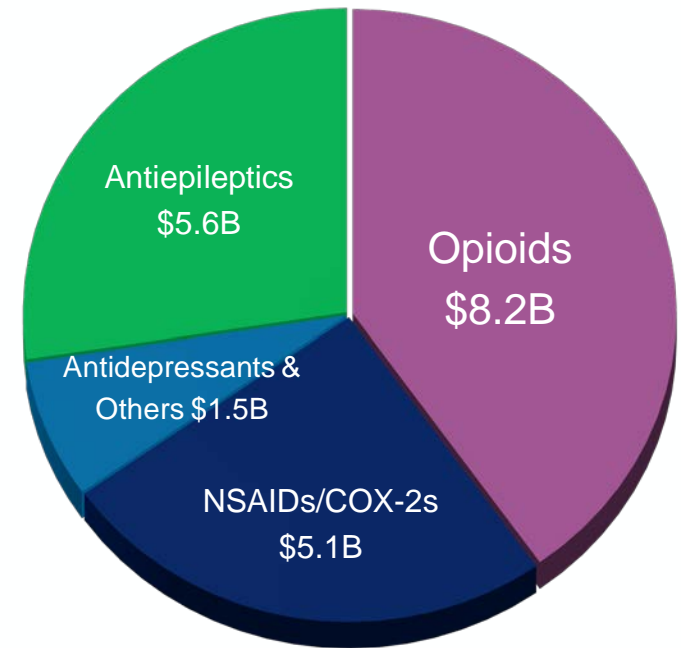
*NDA to be Submitted Q2 2018*

# NKTR-181: A Novel Opioid Poised to Transform the Chronic Pain Market

## NKTR-181 brings unique properties to the treatment of chronic pain:

- ▶ Slow rate of entry into CNS separates pain control from euphoria that leads to abuse and addiction
- ▶ Low levels of sedation, dizziness and respiratory depression
- ▶ Targeting C-III or better scheduling
- ▶ Properties are inherent to molecule
- ▶ Received Fast Track Status from FDA
- ▶ Phase 3 program complete
- ▶ NDA submission planned in Q2 2018

## \$20 Billion+ Global Chronic Pain Therapy Market



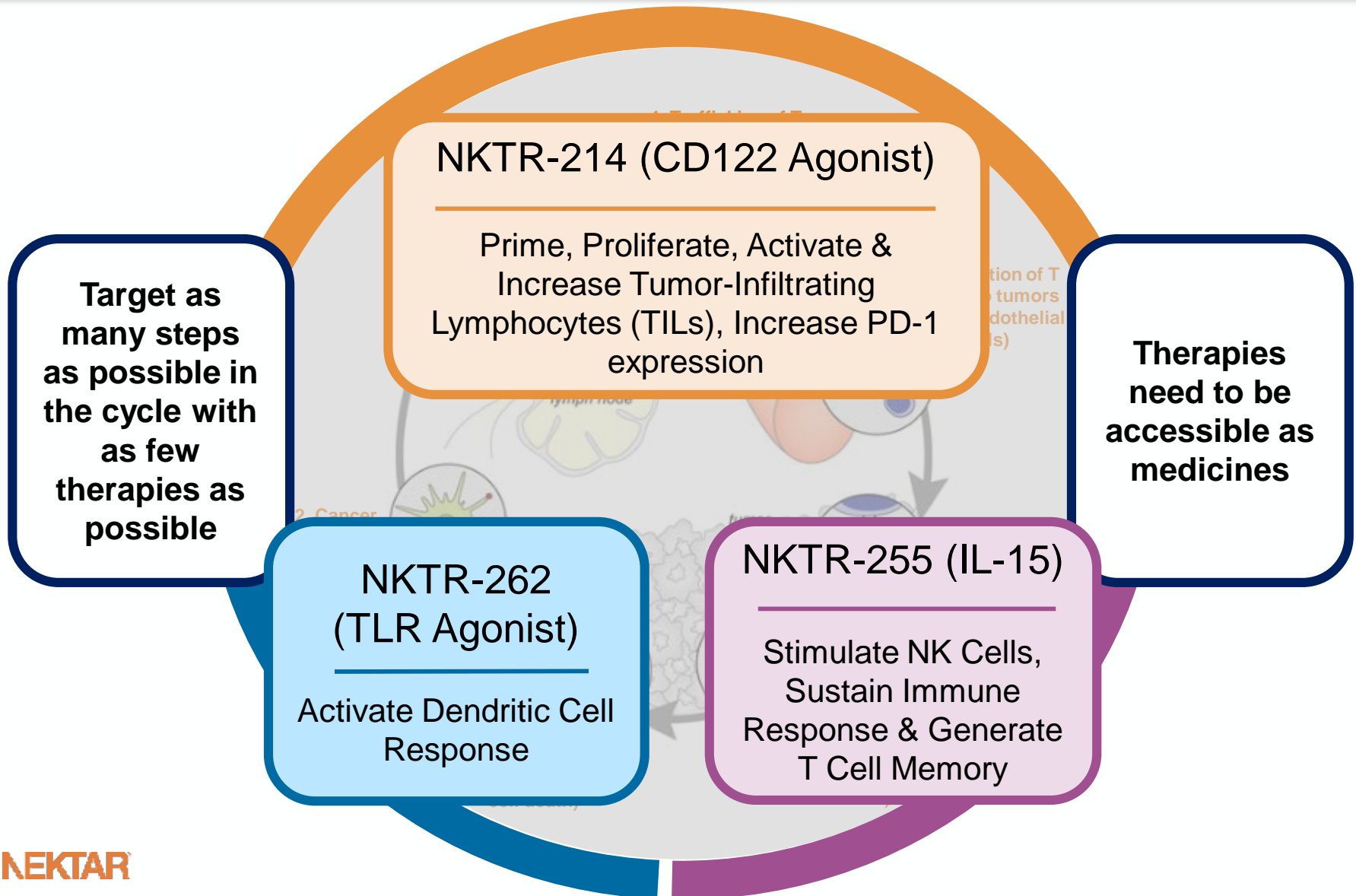
### Chronic pain market includes:

Chronic back pain  
Osteoarthritis  
Fibromyalgia  
Neuropathic pain

# NKTR-181: NDA Submission & Timeline

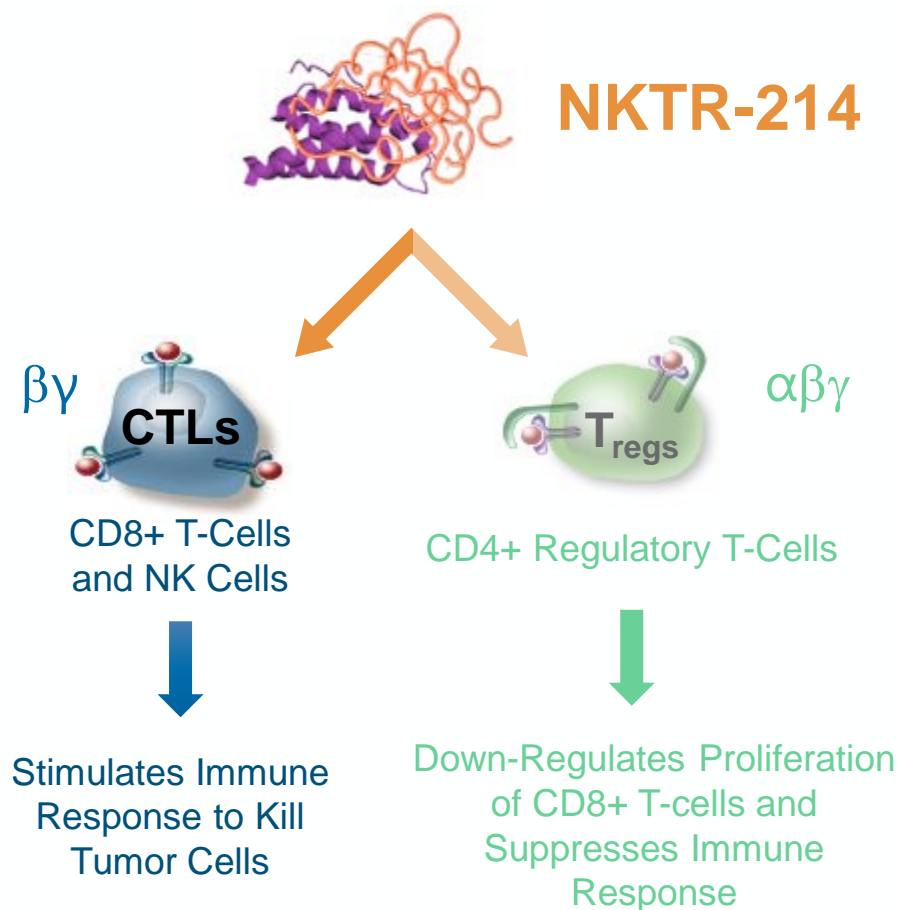
- Two highly productive pre-NDA meetings completed in Q1 2018 with the agency to discuss clinical, nonclinical and CMC data packages that will go into NDA submission
- NDA submission planned in Q2 2018 with extensive efficacy and safety clinical data package:
  - 600-patient efficacy study in patients with chronic pain who are new to opioid therapy
  - 630-patient long-term 52-week safety and efficacy trial in patients who are new to opioid therapy as well as those who are experienced with opioid therapy
  - PK and PD studies in over 450 healthy subjects (therapeutic and suprathreshold NKTR-181 doses)
  - Human abuse potential study of therapeutic and suprathreshold NKTR-181 doses in recreational drug users (tablets)
  - Human abuse potential study of therapeutic NKTR-181 doses in recreational drug users (solution)
- Actively evaluating potential licensing to commercial partners or other strategic structural alternatives while advancing the regulatory process

# Nektar's Immuno-Oncology Strategy to Create Therapies that Cover the Immunity Cycle



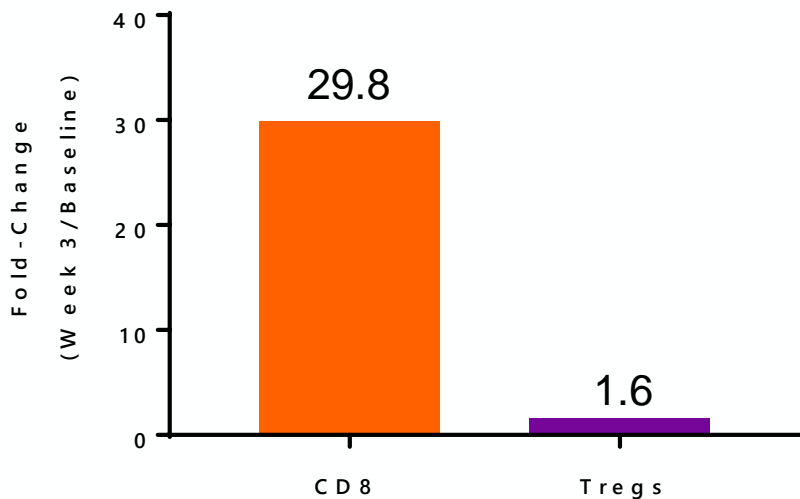
# NKTR-214: Biasing Action to CD 122, or IL-2R Beta, to Stimulate T-Cell Production

- Biases signaling to favor the CD122 Receptor (IL-2R $\beta\gamma$  complex)
- Eliminates over-activation of IL-2 pathway that results in serious safety issues
- Achieves antibody-like dosing schedule in outpatient setting



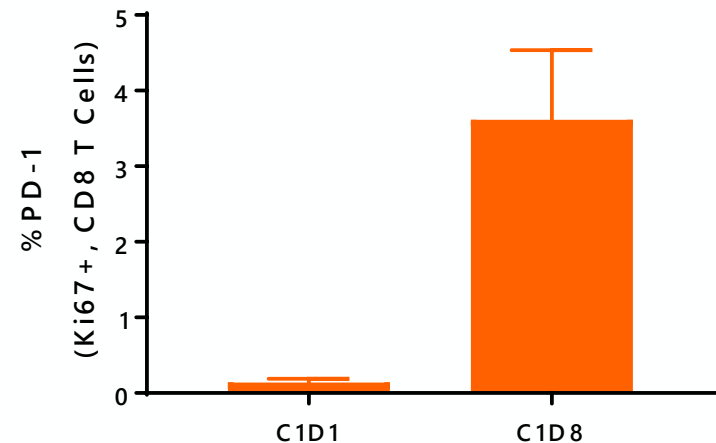
# NKTR-214 Selectively Grows T Cells and Increases PD-1 Expression in Cancer Patients

## Increased T cell Populations in Tumor



Fold Change Expressed as Week 3 / Pre-Dose

## Increased PD-1 Expression on CD8 T Cells



26x Average Fold Increase in PD-1 Expression over Baseline



# Establishing NKTR-214 as a Backbone Immuno-oncology Therapy

## *Global Development & Commercialization Agreement*



Nektar and BMS to pursue >20 indications in 9 tumor types in a Joint Clinical Development Plan with Opdivo and Opdivo plus Yervoy in certain indications

Nektar free to combine NKTR-214 with any agent other than anti-PD-1/PDL-1 in any indication, including third party clinical collaborations

Nektar free to combine NKTR-214 with other PD-1/PD-L1 agents in indications outside of the Joint Clinical Development Plan

# Collaboration Achieves Key Strategic Goals for NKTR-214 Program

- **Substantial upfront and future milestone** economics to Nektar
- Nektar **maintains control** of NKTR-214 (pricing and distribution)
- Nektar **books revenue** for worldwide sales of NKTR-214
- Nektar has **global commercialization rights**
- Nektar **keeps majority of global profits** of NKTR-214 (65%)
- Nektar gains access to resources and infrastructure of Bristol-Myers Squibb to **expedite a broad Phase 3 development program starting middle of 2018**
- **Majority of development costs for broad Phase 3** registration-enabling trials with Opdivo (+/- Yervoy) paid by **Bristol-Myers Squibb**
- Nektar **is free to develop NKTR-214 with other anti-cancer agents** (either our own or those of third parties)

*Allows Us to Rapidly Establish NKTR-214 As Backbone Immuno-oncology Therapy*

# Substantial Upfront and Future Cash Payments

- **Total Up-Front Payments and Milestones to Nektar of \$3.63 Billion**
  - **Total upfront payments of \$1.85 billion**
    - \$1.0 billion upfront cash payment to Nektar
    - \$850 million upfront equity investment in Nektar
      - 8,284,600 shares at \$102.60 per share
      - BMY is subject to standstill agreement
      - BMY has agreed to lock-up provisions and voting provisions for a period of five years
  - **Nektar is eligible for an additional \$1.43 billion in development and regulatory milestones**
    - A total of \$650 million for 1st indication upon filings and launches in US, EU and Japan
    - A total of \$780 million for next 3 indications upon filings and launches in US, EU and Japan (\$260 million total for each indication)
  - **Nektar is eligible for an additional \$350 million in global sales milestones**

# Broad Joint Clinical Development Plan to Rapidly Advance NKTR-214 with Opdivo

## Joint Clinical Development Plan of registration-enabling clinical trials in $\geq 20$ indications in 9 tumor types in ~15,000 patients

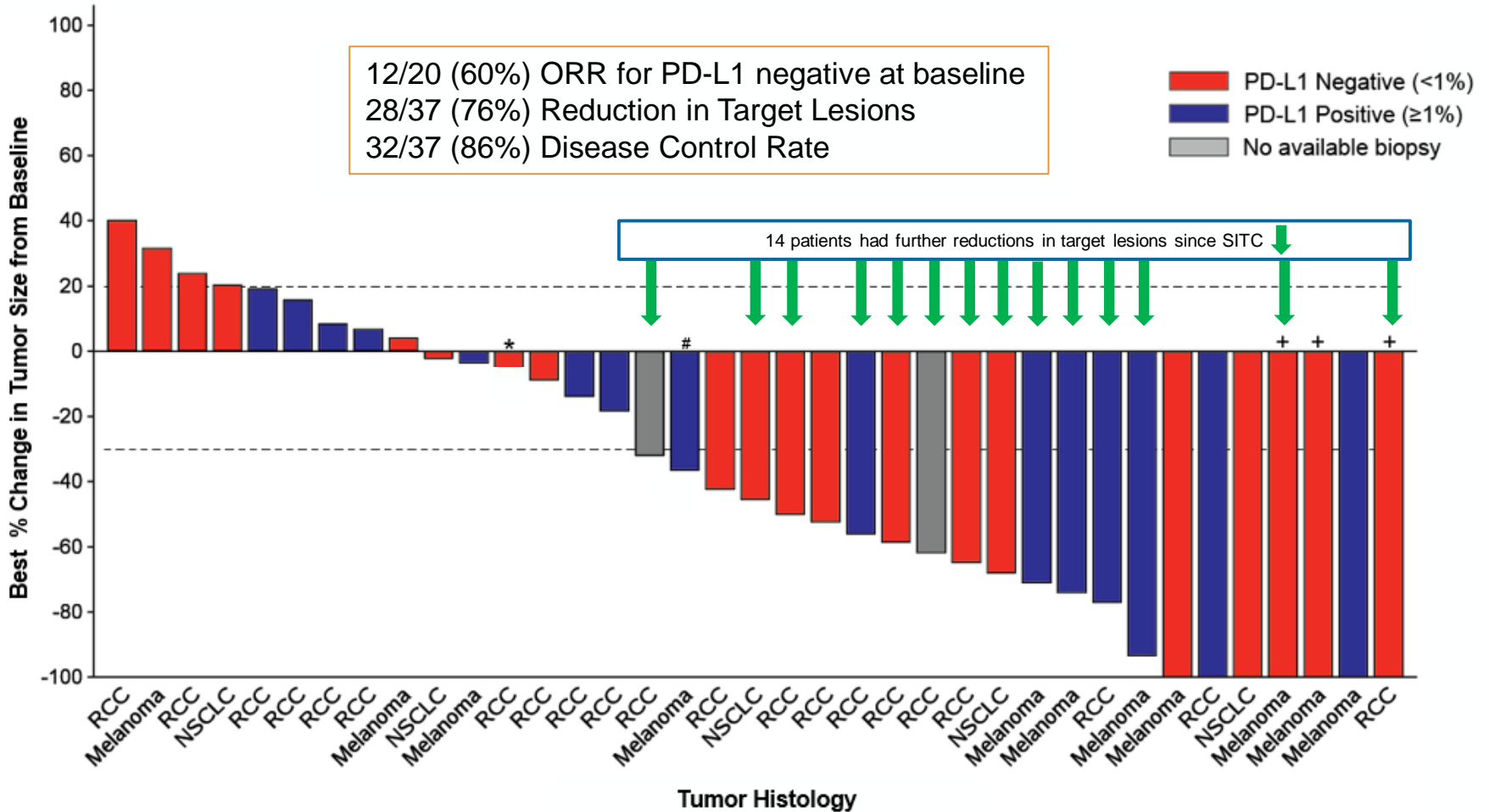
- Registration-enabling studies to start no later than 14 months from effective date of collaboration (subject to allowable delays)
- 9 Tumor Types: Non-Small Cell Lung, Small Cell Lung, Melanoma, Renal Cell Carcinoma, Urothelial, Breast, Colorectal, Gastric, and Sarcoma
- Parties to share development costs of registration-enabling trials as follows:

Combination Therapy	BMJ	NKTR
NKTR-214 + Opdivo	67.5%	32.5%
NKTR-214 + Opdivo + Yervoy	78.0%	22.0%

**Nektar has annual development cost sharing cap of \$125M**



# March 2018: NKTR-214 + Opdivo® Shows Tumor Reduction for Both PD-L1 Negative and Positive Patients (N=37)



\* Best overall response is PD (SD for target lesions, PD per non-target lesions)

# Best overall response is SD (PR for target lesions, PD per new lesion at confirmatory scan)

+ Best overall response is PR (CR for target lesions, non-target lesions still present)

Data are shown for patients with post-baseline scans that included assessment of target lesions.

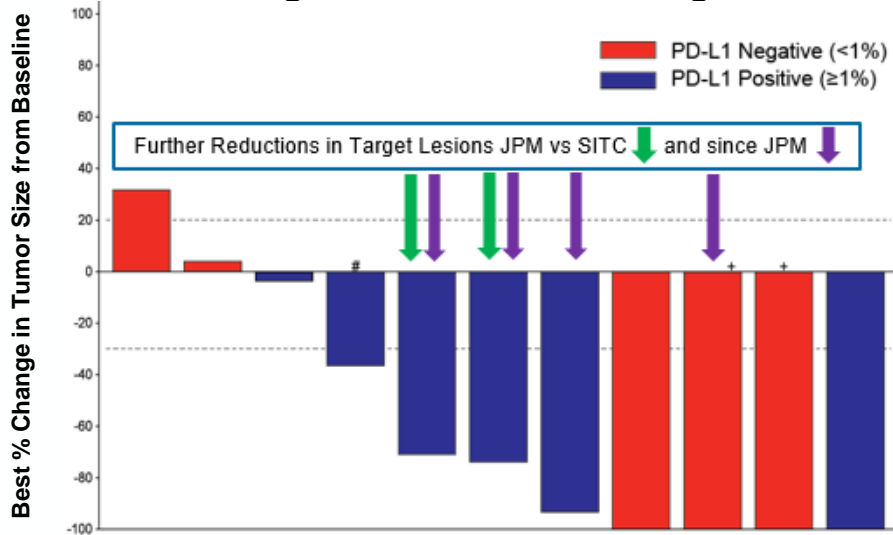
One patient discontinued from study due to clinical progression before the first post-baseline tumor assessment

Source: Data as of March 06, 2018

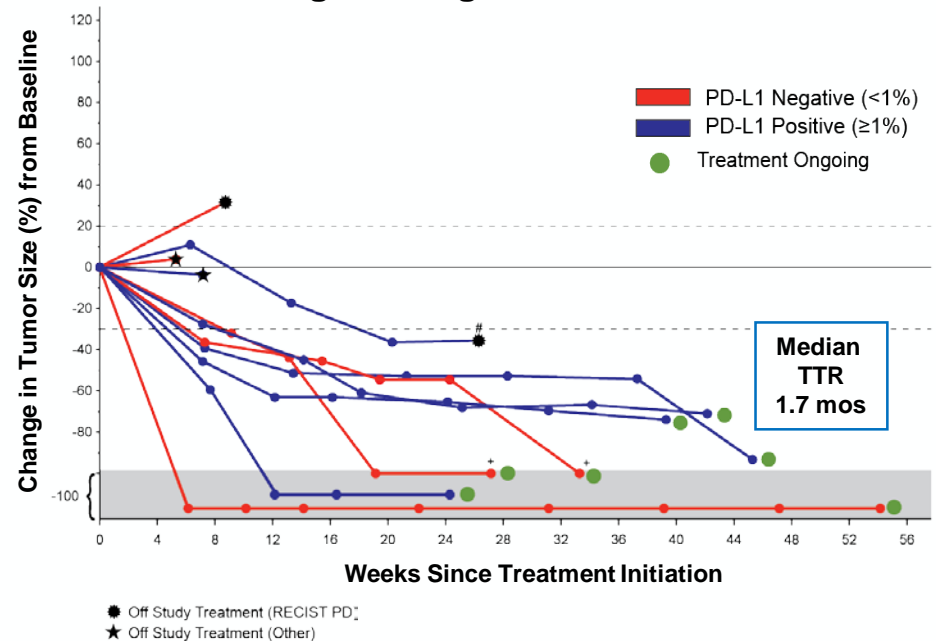
# Stage IV Treatment-Naïve Melanoma Patients (N=11) in PIVOT Dose Escalation

Best Overall Response by RECIST: ORR=7/11 (64%); DCR=10/11 (91%)  
 Best Overall Response by irRECIST: ORR=8/11 (73%); DCR=10/11 (91%)

### % Change From Baseline in Target Lesions



### % Change in Target Lesions Over Time

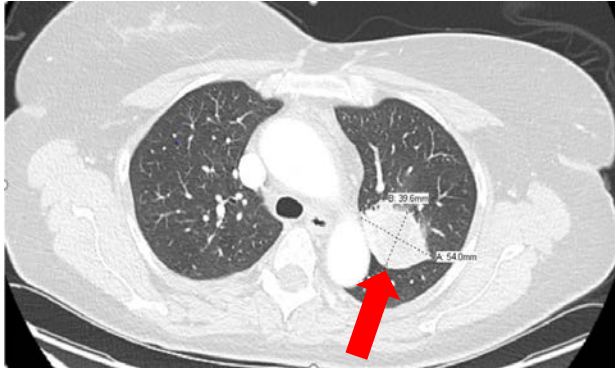


All responses confirmed; ORR is Overall Response Rate  
 DCR is Disease Control Rate  
 TTR is Time to Response  
 + Best Overall response is PR (CR for target lesions, non-target lesions still present)  
 # Best Overall Response is SD (PR for target lesions, PD per new lesion on confirmatory scan)  
 Source: Data as of March 06, 2018

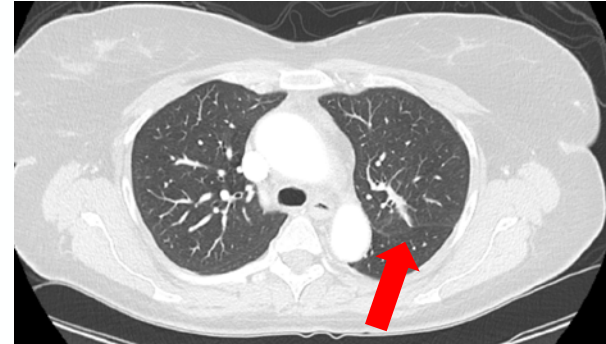
# Patient with 1L Metastatic Melanoma

## Age 63, PD-L1(+)

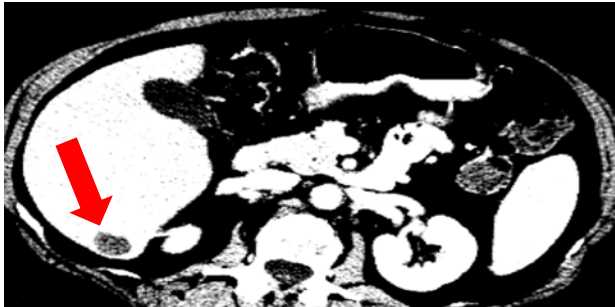
Lung Lesion, 54 mm



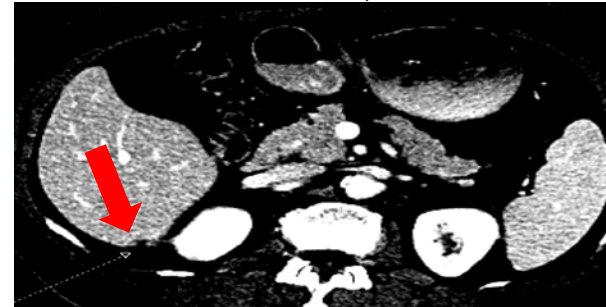
Lung Lesion, Undetectable



Liver Lesion, 20 mm



Liver Lesion, 5 mm



Baseline

46 Weeks

- Burden of Disease at Baseline: 74 mm
- Best Overall Response: Confirmed PR (-93%)

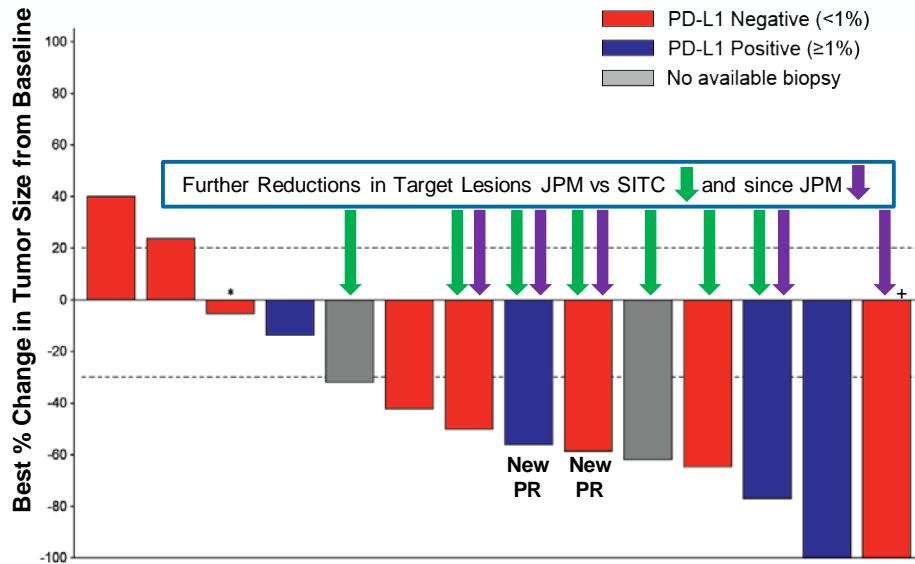
Source: Data as of March 06, 2018



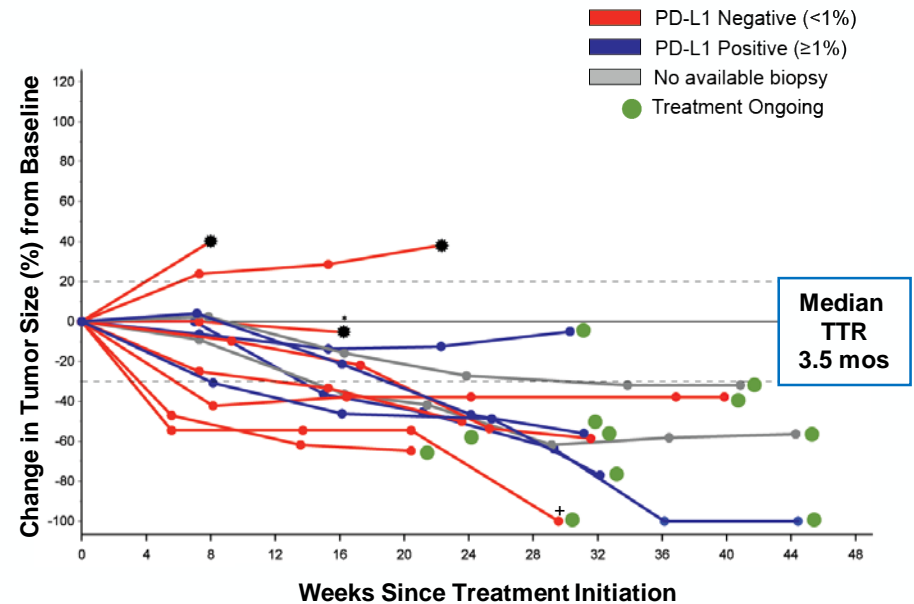
# Stage IV Treatment-Naïve 1L Renal Cell Carcinoma (N=14) in PIVOT Dose Escalation

Best ORR by RECIST : ORR=10/14 (71%); DCR=11/14 (79%)

% Change From Baseline in Target Lesions



% Change in Target Lesions Over Time



All responses confirmed; ORR is Overall Response Rate

DCR is Disease Control Rate

TTR is Time to Response

\* Best overall response is PD (SD for target lesions, PD per non-target lesions).

+ Best Overall response is PR (CR for target lesions, non-target lesions still present)

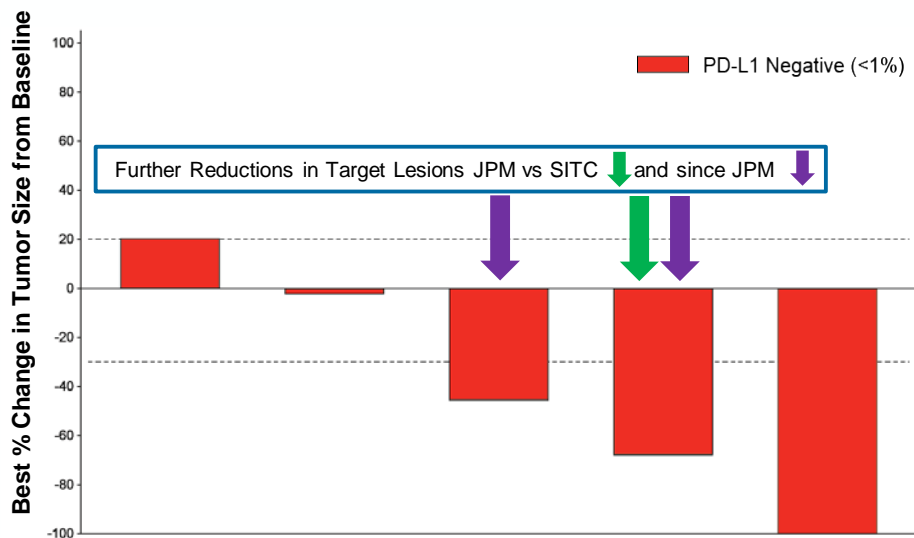
Source: Data as of March 06, 2018



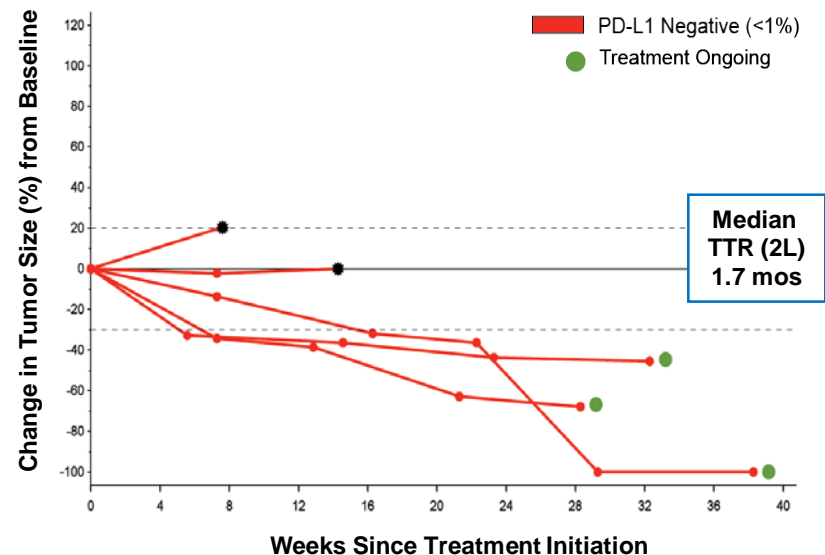
# Stage IV IO-Naïve PD-L1 Negative NSCLC 1L and 2L (N=5) in PIVOT Dose Escalation

Best Overall Response by RECIST (2L): ORR=3/4 (75%); DCR=3/4 (75%)

### % Change From Baseline in Target Lesions



### % Change in Target Lesions Over Time



All responses confirmed; ORR is Overall Response Rate  
DCR is Disease Control Rate  
TTR is Time to Response  
Source: Data as of March 06, 2018

● Off Study Treatment (RECIST PD)

# Key Takeaways from Dose Escalation Stage of PIVOT

## Efficacy

- Compelling ORR and DCR in both PD-L1 negative and PD-L1 positive patients
- 100% of patients with responses continue to be responders and continue on treatment with no relapses
- More responses observed over time (1L RCC)
- Deepening responses observed over time on treatment

## Safety and Tolerability

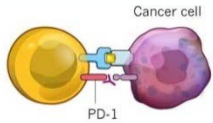
- Convenient and well-tolerated outpatient dosing schedule once every 3 weeks
- Lowering of imAEs compared to checkpoint inhibitors in single agent and combination regimens
- Most common G1/2 side effects were flu-like symptoms that were predictable, short lived and easily managed
- Low G3 TRAE rate of 10.5% with no discontinuations from TRAEs and no treatment related deaths

## Biomarkers

- Tumor infiltrating lymphocyte levels increase significantly after the start of treatment with NKTR-214 + Nivolumab

# NKTR-214: Development Program in 2018

## Checkpoint Inhibitors



Ongoing PIVOT Study of NKTR-214 Plus Opdivo® in Melanoma, RCC, NSCLC, Bladder, TNBC, Colorectal, Gastric, SCLC (Nektar & Bristol-Myers Squibb)

Phase 3 Studies in 1L Melanoma and 1L Renal Cell Carcinoma to Start Mid-2018 (NKTR-214 plus Opdivo®)

Ongoing PROPEL Study of NKTR-214 with Keytruda® or Tecentriq® (Nektar)

Ongoing IST in Sarcoma with NKTR-214 with Opdivo® at MSK and MD Anderson (Nektar & Bristol-Myers Squibb)

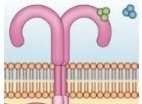
Phase 1 trial NKTR-214 with NKTR-262 (IND Filed YE2017, Dosing Q12018)

Preclinical studies of NKTR-214 with adoptive T-cell therapies

Preclinical studies underway with 5 clinical compounds with Takeda in liquid and solid tumors

Preclinical studies underway with vaccines

## TLR Agonist

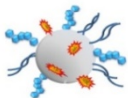


## Cell Therapies



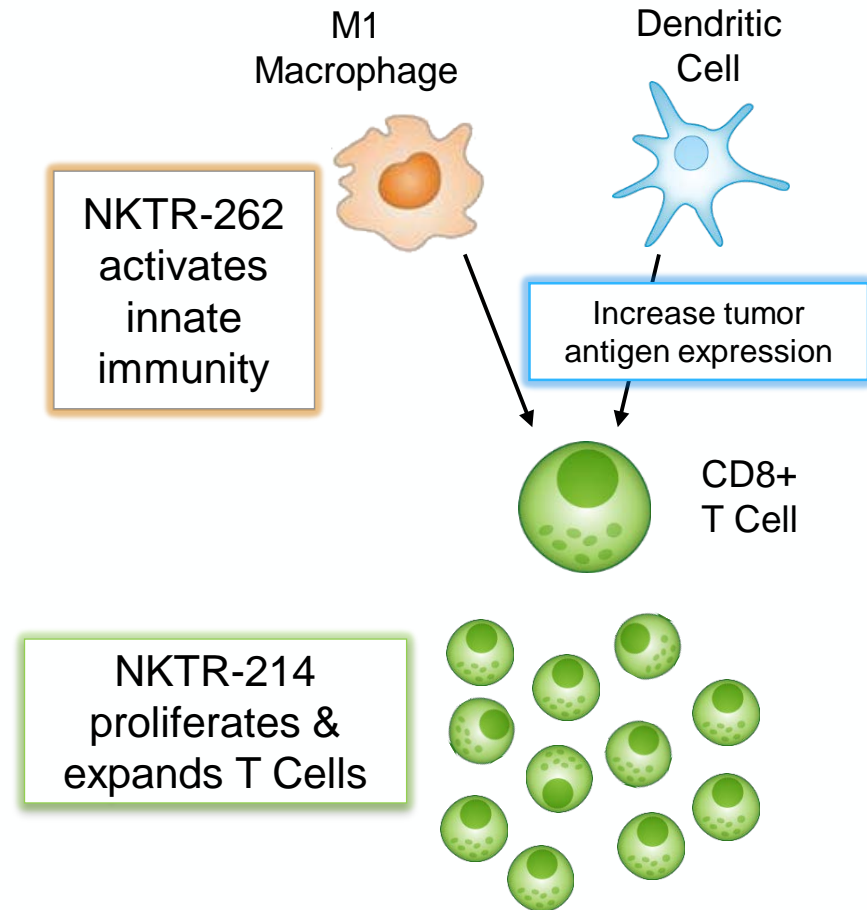
## Small Molecules

## Vaccines

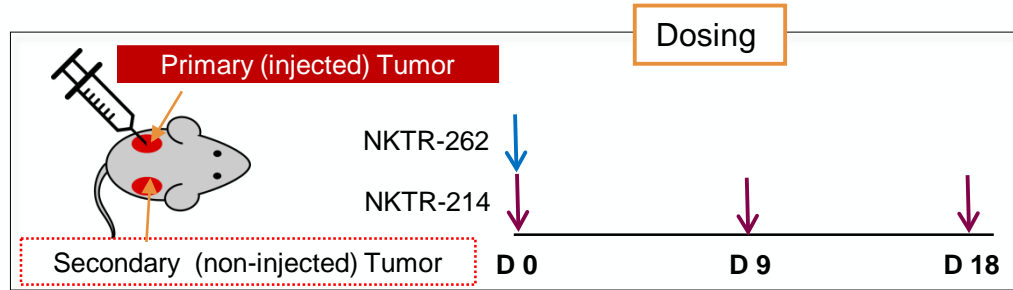


# NKTR-262: A Unique Intratumoral TLR Agonist to Target the Innate Immune Response

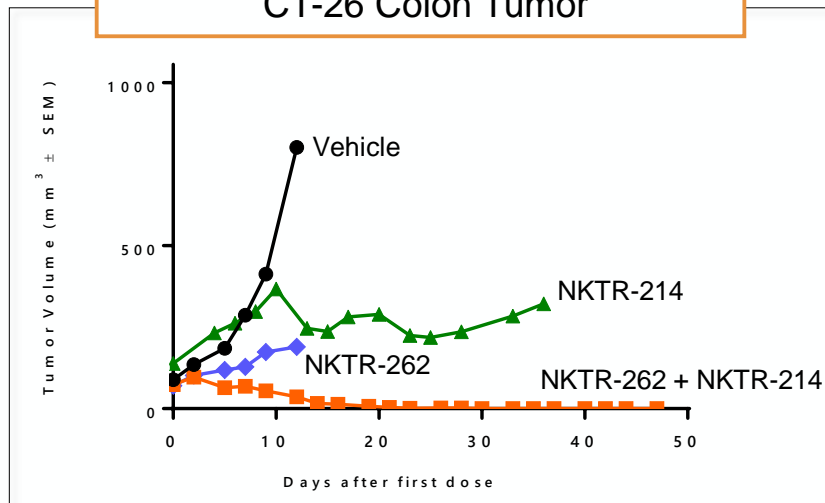
- Activates myeloid cell response and increases tumor antigen presentation
  - Overcomes tumor-suppressing micro-environment by mimicking local infection
- NKTR-262 designed to be synergistic with NKTR-214 and is a novel, wholly-owned I-O combination for Nektar
- Nektar technology optimizes abscopal anti-tumor effects with minimal systemic exposure
- IND Filed End of 2017
- Phase 1 Dosing To Start in March 2018



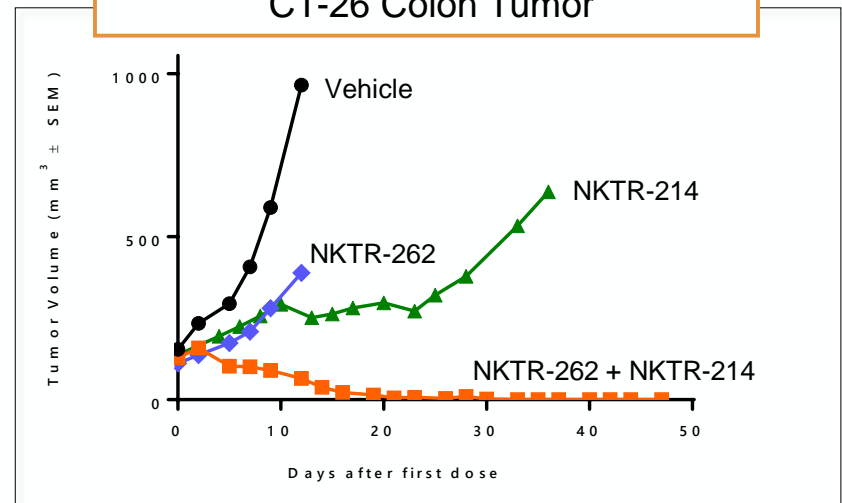
# Complete Regression and Abscopal Effect with Combination of NKTR-262 and NKTR-214



**Primary (injected) CT-26 Colon Tumor**

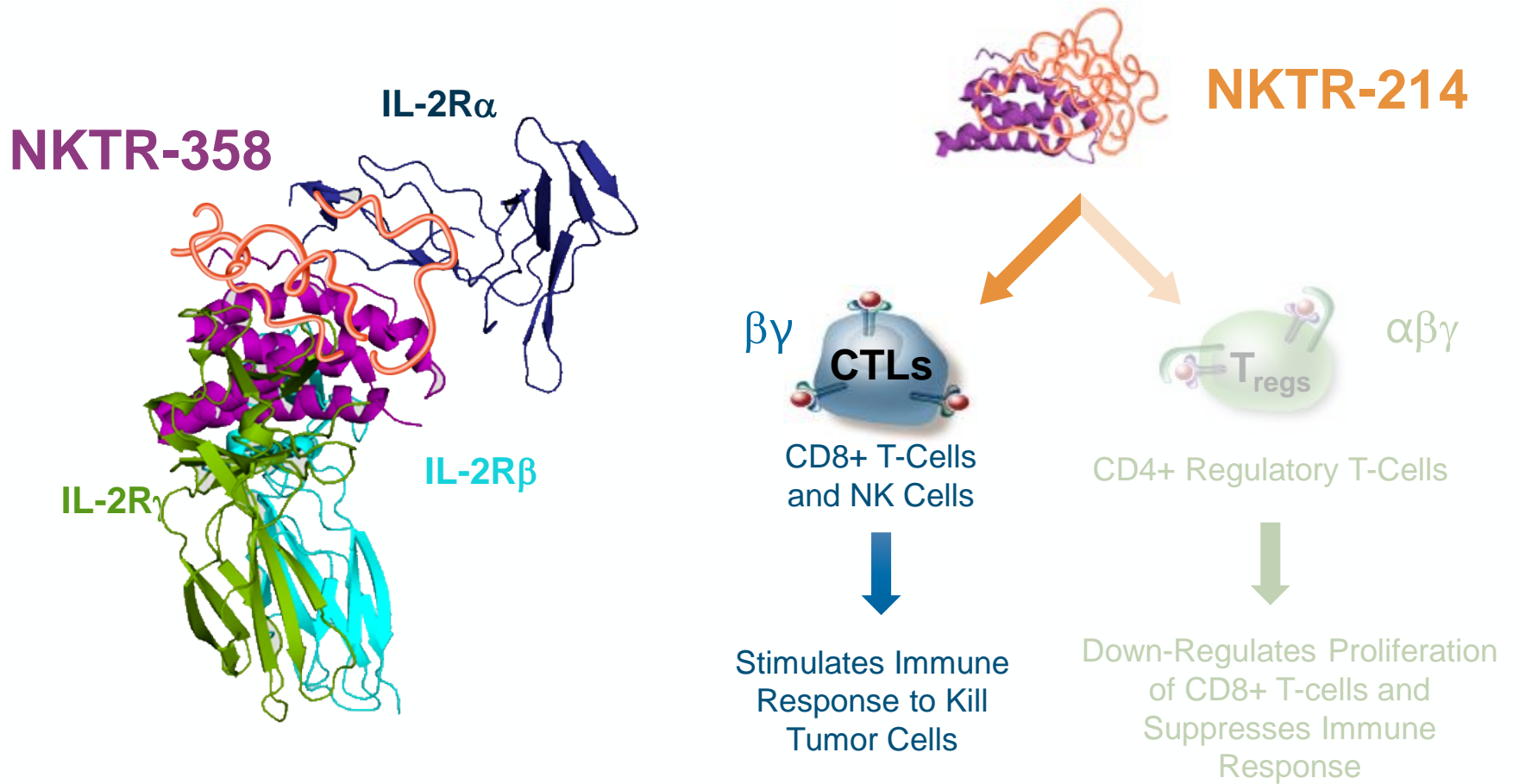


**Secondary (non-injected) CT-26 Colon Tumor**

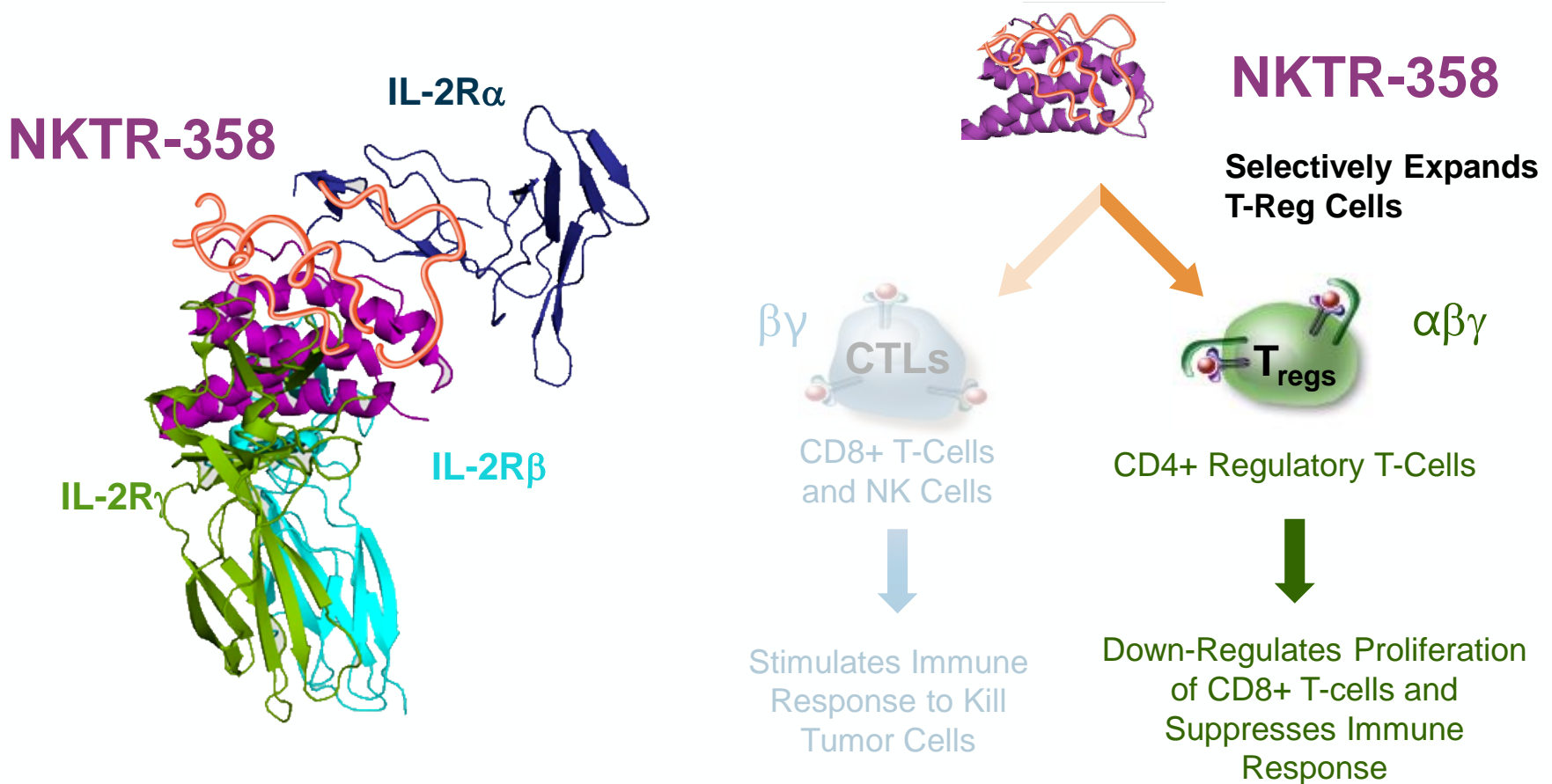


NKTR-262 0.8 mg in 40  $\mu$ L volume given in a single IT dose, NKTR-214 0.8 mg/kg q9dx3 IV; N=10 per group

# NKTR-358: A T Regulatory Stimulatory Agent



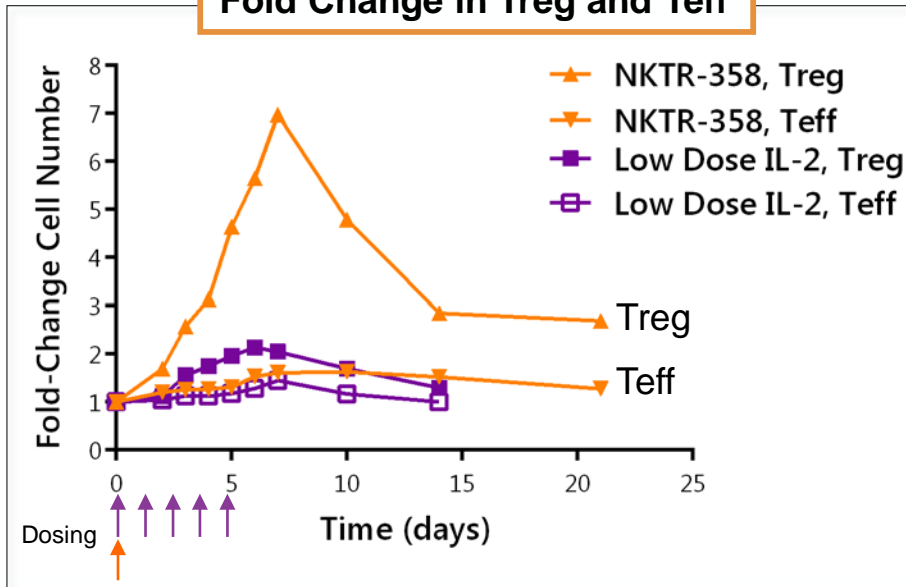
# NKTR-358: Increases T Regulatory Cells and Their Suppressive Activity



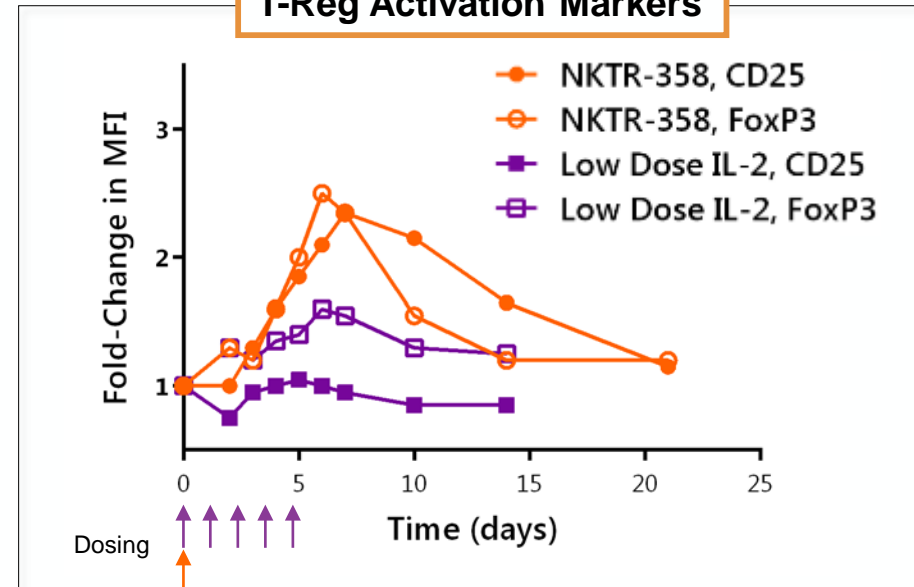


# NKTR-358 is Selective for Enhancing of T-Reg Proliferation and Activation in Non-Human Primates

### Fold Change in Treg and Teff



### T-Reg Activation Markers



- ▶ Single dose NKTR-358 produced greater Treg expansion than repeat low-dose IL-2
- ▶ In mice, NKTR-358 treatment promotes >30-fold increase in Treg suppressive activity

1M + 1F cynomolgus monkey per treatment, both agents given at 0.025 mg/kg – single dose SC for NKTR-358 vs QDx5 SC for IL-2.

# Second Clinical Study of NKTR-358 to Start in 1H 2018 in Healthy Subjects and Patients with Lupus

- Ongoing first-in-human study shows multiple-fold increase in T regulatory cells with no increase in CD8+ or NK cells following single doses of NKTR-358
- No dose-limiting toxicities to-date
- Data from Phase 1 single ascending dose study planned for potential presentation at medical meeting in 2018
- Initiating Phase 1 multiple dose ascending study in patients with lupus in 1H 2018
- NKTR-358 has potential to be developed as first-in-class resolution therapeutic in lupus, Crohn's disease, rheumatoid arthritis, psoriasis and transplant patients

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